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The Reductive Coupling of 2-Cyanopyrroles: A Study Pertaining to the Mechanism of Formation of Porphocyanines

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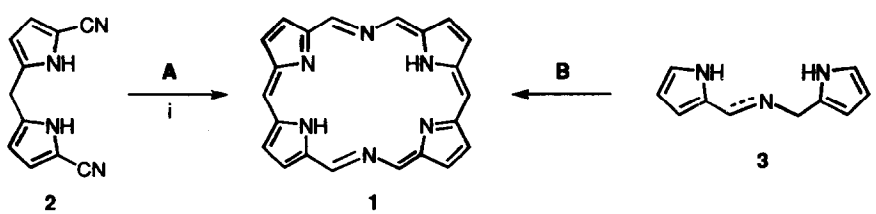
Abstract: 2-Cyanopyrrole was found to form (2-pyrrolylmethene)-(2-pyrrolylmethyl)imine when treated with lithium aluminum hydride (LAH), followed by a mild work-up. A plausible mechanism of this reductive coupling was inferred from a series of experiments, including ^{27}Al-NMR, deuteration experiments, and the reduction of variously substituted cyanopyrroles. The mechanism, a metal chelate mediated dimerization, may be the key to understanding porphocyanine synthesis *via* the LAH reduction of 1,9-dicyanodipyrromethanes.

INTRODUCTION

The synthesis of long-wavelength absorbing pyrrolic pigments for potential use in photodynamic therapy (PDT) is currently an active area of research.[2] We contributed to this field recently by reporting on the synthesis of a novel class of expanded porphyrins.[3-5] These tetrapyrrolic, imine containing pigments were named porphocyanines (**1**) and two alternative methods for their synthesis have been found since the initial report. In particular, the synthesis by an *in situ* oxidation of the lithium aluminum hydride (LAH) reduction product of 1,9-dicyano substituted dipyrromethanes is simple and efficient (yields over 30% are commonly observed). However, details of the mechanism of this effective formation of the macrocycle remained unclear (Scheme 1, Pathway A).[3]



2 1 3

Reaction conditions: (i) 1. LAH, 2. H_2O, 3. oxidation (DDQ or O_2)

Scheme 1

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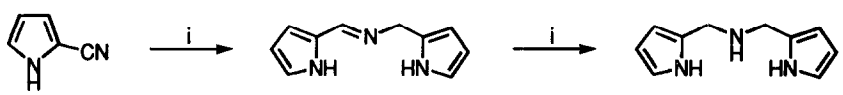
Recently, we have investigated alternative routes attempting to form the macrocycle by establishing carbon links between nitrogen-linked dipyrrolic molecules such as **3** (Scheme 1, Pathway **B**), thereby essentially reversing the order of bond formations compared to the earlier syntheses. During the course of this work, we discovered that LAH induces the reductive coupling of 2-cyanopyrroles to provide a simple and efficient synthesis of (2-pyrrolylmethene)-(2-pyrrolylmethyl)imines. This and the experiments towards the elucidation of the mechanism of this coupling are described here. These findings, in turn, shed light onto the mechanism of the porphocyanine formation along the cyanodipyrromethane reduction pathway **A**. We also report the synthesis of some new mono- and dicyanopyrroles used in the coupling studies.

RESULTS AND DISCUSSION

We chose (2-pyrrolylmethene)-(2-pyrrolylmethyl)imine (**4**), previously prepared by reaction of 2-(aminomethyl)pyrrole with 2-formylpyrrole, as a starting material for a potential formation of porphocyanine along pathway **B**.[6] 2-Aminomethylpyrrole was reportedly synthesized by the LAH reduction of 2-cyanopyrrole (**5**).[7] When we repeated these procedures, we replaced the aqueous quenching (2.5 M sulfuric acid) of the LAH reduction reaction mixture by the addition of Glauber's salt ($Na_2SO_4 \cdot 10\,H_2O$). Surprisingly, we found that imine **4** was formed as the sole product in 85% isolated yield (Scheme 2). This finding, contrary to earlier reports (*vide infra*), is limited to the use of aluminum hydrides as reductant. Cyanopyrrole **5** is inert to sodium borohydride, with or without the addition of transition metals,[8] but we found also that diisobutylaluminum hydride (DIBAL) produced **4**, albeit not as cleanly (less than 50% yield). The formation of **4** was also surprising since its imine linkage is susceptible to reduction by LAH under the reaction conditions used for its formation, thereby providing amine **6** (Scheme 2).



5 **4** **6**

Reaction conditions: (i) 1. LAH, 2. H_2O

Scheme 2

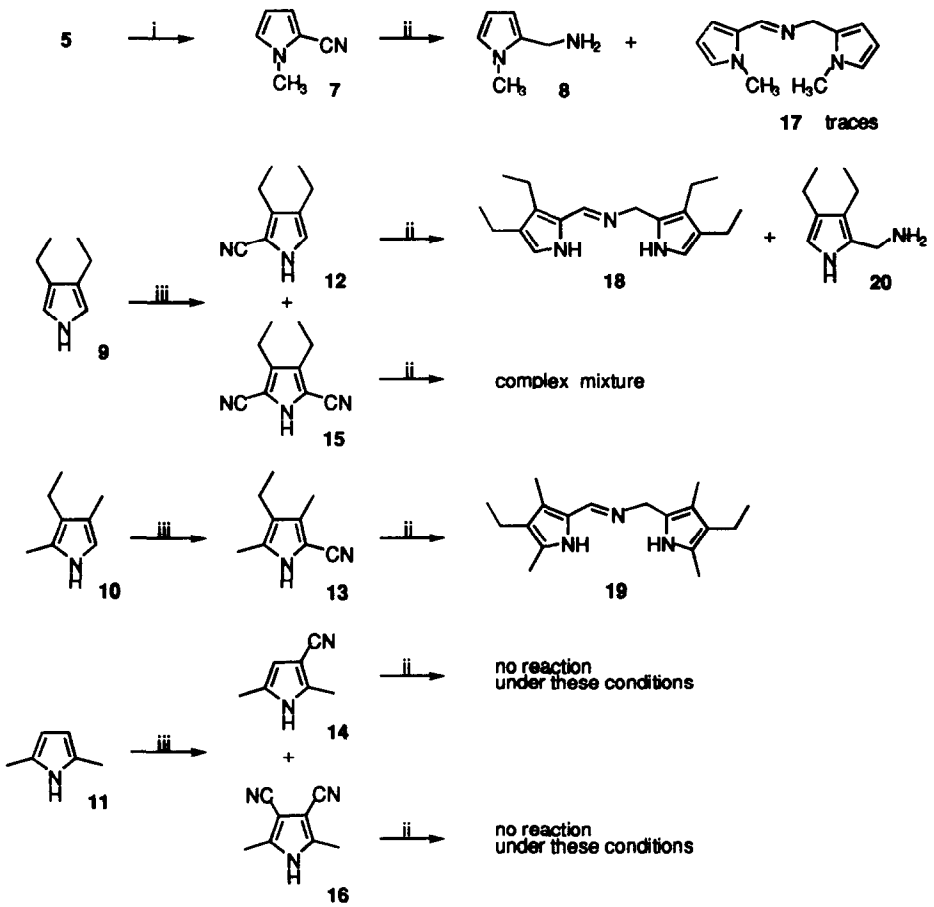
The arsenal of methodologies to create imine linkages is exeedingly rich.[9] Under special conditions (reductant in aqueous acid), 2-cyanopyrroles can be reduced to bis-2-pyrrolyl aldimines. However, they are hydrolyzed *in situ* under these conditions to the corresponding 2-pyrrole aldehydes.[10] Aromatic aldimines are also known to condense to form imine linked dimers. One example of the latter reaction is the formation of hydrobenzamide $ArCH(-N{=}CHAr)_2$ from an aryl aldehyde and ammonia *via* the imine $ArCH{=}NH$.[11,12] However, such an explanation, for the formation of **4** by LAH reduction of 2-cyanopyrrole (**5**), suffers several deficiencies. Firstly, the special reaction conditions for the partial cyano group reductions are not met, nor is 2-cyanopyrrole electronically as deactivated as 2,4-dicyanopyrrole, another instance in which partial reduction has been observed.[7,13] Secondly, the reduction of 2-cyano-1-methylpyrrole (**7**) gave predominantly the 2-(aminomethyl)pyrrole **8** (Scheme 3). This finding then, given the electronic similarities of **7** and **5**, is surprising. Another mechanism can be suggested. A portion of the cyanopyrrole (**5**) was fully reduced to the aminomethyl compound, the remainder was partially reduced to the aldimine. Upon hydrolysis, the latter formed the aldehyde and immediately reacted with the aminomethylpyrrole to form the observed imine. Such *in situ* formation of imines, albeit in the absence of

LAH, have been observed before.[14] In our case, such a mechanism can be excluded. The inability to explain the observed stoichiometry in the presence of excess reductant is, perhaps, the strongest argument against this mechanism. Our observations suggest, however, an LAH mediated *in situ* reductive coupling mechanism.

To investigate this hypothesis in more detail, several cyanopyrroles were synthesized and their behavior towards the LAH reduction conditions were studied.

Synthesis of Cyanopyrroles

Cyanopyrroles are available by a variety of methods.[7,15] Possibly the most versatile and convenient strategy is the direct introduction of cyano groups by reaction of a pyrrole with chlorosulfonyl isocyanate (CSI)[16] followed by solvolysis of the intermediate chlorosulfonylamide with DMF.[7,17,18] This methodology was applied to 3,4-diethylpyrrole (**9**), 3-ethyl-2,4-dimethylpyrrole (**10**)[19] and 2,5-dimethylpyrrole (**11**), to produce, in good yields, the monocyanopyrroles **12**, **13**, and **14** (Scheme 3).



Reaction conditions: (i) 1. KH, 2. CH_3I; (ii) $LiAlH_4$, then $Na_2SO_4 \cdot 10\ H_2O$; (iii) CSI/DMF/CH_3CN, aqueous workup

Scheme 3

2-Cyanopyrrole (**5**) was converted to the known 1-methyl-2-cyanopyrrole (**7**)[20] by methylation of the pyrrolic nitrogen. In cases where two pyrrolic hydrogens could be substituted for cyano groups, the dicyanopyrroles (**15** and **16**) were observed as by-products. By use of a 2.5 fold stoichiometric excess of CSI, the doubly cyanated pyrroles became the major products, a finding similar to that described for pyrrole.[18]

LAH Reduction of the Cyanopyrroles

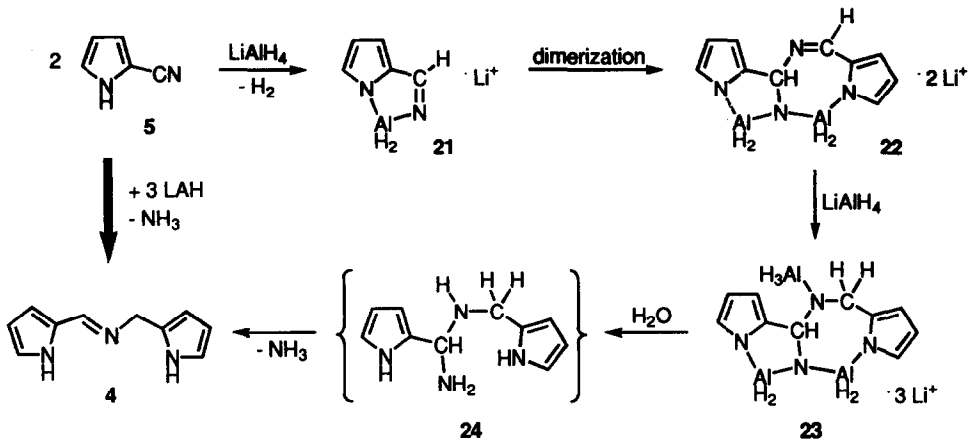
The cyanopyrrole was dissolved in dry THF, and to the cooled solution were added, under anhydrous conditions, four equivalents of LAH. The mixture was then stirred for one hour. Glauber's salt was then added in portions until gas evolution ceased. The resulting slurry was filtered through Celite®, the filtrate was evaporated, *in vacuo*, and the residue analyzed by TLC, mass spectrometry, ^{1}H- and ^{13}C-NMR spectroscopy. The results are summarized in Schemes 2 and 3.

The reduction of 2-cyanopyrrole (**5**) produced exclusively the dimer imine **4**. Reductions performed with less reductant than required for full conversion of the starting material and quantification of the reaction mixture by ^{1}H-NMR revealed a limiting stoichiometry of 1.8 (± 0.3) LAH per cyanopyrrole. Experiments with LAH-d_4 proved the origin of both the methylene and the methine proton to be the reductant. The protons of the methine-linked pyrrole unit and, naturally, the NH protons exchange under the strongly basic conditions of the quenching step, i.e., an LAH-d_4 reduction with quenching with D_2O (in form of deuterated Glauber's salt made by diffusion of D_2O onto anhydrous Na_2SO_4) produced **4** in which these protons were partially deuterated.

Reduction of cyanopyrrole **7** resulted almost exclusively in the formation of the corresponding aminomethyl compound **8**, and only a small amount of the dimer **17** was observed (product ratio of at least 13:1 in favor of **8**). Reduction of compound **12** gave the imine dimer **18** and the aminomethyl pyrrole **20**. The ratio of the two compounds **18** and **20** varied from run to run from 1:2 to 1:3. Reduction of cyanopyrrole **13** produced the imine **19** as the sole product. The reduction of dicyanopyrrole **15** was slow and produced an unidentified complex (polymeric ?) mixture. ß-Cyanopyrroles **14** and **16** resisted reduction under the conditions employed and were recovered unchanged. This stability of ß-cyano groups towards nucleophilic attack has been reported.[7]

The major difference between starting materials, in these reductions, is the ability of their pyrrole-nitrogens to coordinate with the reductant. The N-methylated pyrrole **7** cannot readily coordinate with aluminum. In order to trace possible aluminum complexes formed by (partially reduced) **5** and LAH, ^{27}Al-NMR spectra of solutions of **5** (0.5 M) in THF/benzene-d_6 (19:1) containing defined amounts of LAH were measured. With roughly a 1:2 ratio of **5**:LAH, a sharp strong signal for the LAH and a broad featureless signal from 20 ppm downfield to 40 ppm upfield were seen. Increasing the relative amount of **5** strengthens the broad signal at the expense of the LAH signal and shifts it gradually upfield. At about a 2:3 ratio the LAH signal vanished entirely and only one broad signal 20-80 ppm upfield (of the external LAH reference signal) is visible. This signal sharpens up a little but does not shift any further at higher pyrrole:LAH ratios. Failure to measure well defined signals for the presumed aluminum complex is, due to the quadrupole moment of the ^{27}Al-nucleus, not unexpected. Only highly symmetric (tetrahedral) complexes exhibit sharp signals.[20] The experiments nevertheless supported the assumption of formation of a 2:3 cyanopyrrole:LAH complex.

The literature reveals two closely related reductions.[22] The more recent contribution by Wang and Sukeniki describes the reduction of benzaldoximes with LAH in HMPA-containing solvents to give benzylidene-benzylimine. The mechanism we propose for the reductive dimerization of cyanopyrroles is reminiscent to that of the benzaldoxime reductive dimerization in that the reductant acts as base as well as reductant (Scheme 4).



For simplification, the aluminum is depicted as a tetracoordinated species. This does not imply, however, that the solvent does not coordinate to give higher coordinated species.

Scheme 4

Accordingly, the first step would be a combined deprotonation/reduction of **5** to form a chelate of type **21**. Similarly constructed chelates of copper(II) are known for 2-pyrrolealdehyde.[23] This chelate may dimerize to give complex **22**. Its imine double bond may be reduced by another equivalent of LAH to produce compound **23**, at which point no further reduction can occur. Hydrolysis of **23** would give the labile species **24** which upon loss of ammonia gives the final stable product **4**. Ammonia can be detected during the hydrolysis step. The proposed mechanism is consistent with the experimental observations. This mechanism may compete with other mechanisms as indicated by the presence of dimer **18** and the aminomethylpyrrole **20**. This suggests that steric effects may determine which mechanism predominates. Experiments in which equimolar mixtures of **5** and **13** were reduced and quenched, produced complex mixtures. Experiments in which equimolar amounts of **5** and **13** were separately reduced and mixed just prior to the quenching step also produced complex mixtures. These experiments failed to provide evidence for the formation of a single stable intermediate complex. Rather, the presence of several complexes in equilibrium with each other is suggested. These suggestions are not in contradiction to the proposed mechanism.

Attempts to use either imine **4** or amine **6** as building blocks for an alternative porphocyanine synthesis according to route **B** in Scheme 1, and following the general procedures for acid catalyzed cyclizations of dipyrromethanes with benzaldehyde or formaldehyde failed. In the reactions with **4**, this can be understood by the electronic deactivation of the imine substituted pyrrolic unit. The failure of the experiments with **6** might be attributed to either the known fragility of non-ß-alkyl substituted porphocyanine[4] or, equally likely, this may highlight the importance of the metal template-directed dimerization of the subunits for the success of the porphocyanine synthesis by reduction of dicyanodipyrromethanes. Indeed, template effects have been utilized in the synthesis of a wide variety of pyrrolic macrocycles.[24]

The reductive coupling of 2-cyanopyrroles might prove to be useful in the formation of, for example, imine functionalized pyrrolic ligands for metal binding studies[25] or the synthesis of novel ligands.[26] There are indications in the literature that this coupling has been observed before, but went unrecognized. Barnett *et al.* described in 1980 the LAH reduction of 2,4-dicyanopyrroles.[7] Following a workup employing 2.5 M sulfuric acid, they found one product to be 4-cyano-2-pyrrolecarboxaldehyde.

They noted "Over half the starting material was not accounted for."[7] In light of our findings this is understandable. The strong acid hydrolyzed the initially formed imine into a stable pyrrolealdehyde and a very unstable aminomethyl fraction. The latter decomposed and, hence, could not be accounted for.

ACKNOWLEDGMENTS

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EXPERIMENTAL SECTION

Instrumentation and Materials

Melting points were determined on a Thomas Model 40 Micro Hot Stage and are uncorrected. The ^{1}H-NMR and ^{13}C-NMR spectra were measured on a Bruker AC-200 spectrometer with data processing on a Bruker data station and were referenced to residual solvent peaks. The ^{27}Al-NMR were measured on a Varian XL-300 spectrometer referenced to LAH. The low and high resolution FAB and EI mass spectra were obtained on a AEI MS902 and a Kratos MS50 spectrometer. Elemental analyses were performed on a Fisons CHN/O Analyzer, Model 1108 by the departmental Microanalytical Laboratory. The silica gel used in the flash chromatographies was Merck Silica Gel 60, 230-400 mesh whilst Rf-values were measured on Merck silica TLC aluminum sheets (silica gel 60 F_{254}). Unless specified, all reagents and solvents were commercially available and of reagent grade or higher.

Preparation of Compounds

2-Cyano-1-methylpyrrole (7). This compound has previously been prepared. For instance, Barnett *et al.*[7] prepared it in 67% yield by reaction of CSI with 1-methylpyrrole. We prepared **7** in 61% yield by methylating **5**, as its K^{+} salt, with methyl iodide according to a procedure adapted from Ramasay *et al.*[27] The spectroscopic data provided here complement the analytical data provided by Barnett *et al.*[7] or Anderson[20]: R_f = 0.71 (silica-$CHCl_3$); ^{1}H-NMR (200 MHz,) δ 3.72 (s, 3H), 6.10 (dd, *J* = 4.0, 4.0 Hz, 1H), 6.78 (dd, *J* = 4.0, 2.0 Hz, 1H), 6.71 (m, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 35.2, 104.3, 109.4, 113.8, 119.8, 127.6; MS (EI, 150°C) *m/e* 106 (100, M^{+}), 105 (82.0, M^{+}-H), 78 (31.0), 64 (12.3), 52 (14.0); HR-MS (EI, 150°C) *m/e* calc'd for $C_6H_6N_2$: 106.05310, found 106.05302.

Bis(2-pyrrolylmethyl)amine (6). (2-Pyrrolylmethene)-(2-pyrrolylmethyl)imine (**4**) (0.10 g, 0.58 mmol) dissolved in THF (10 mL) was added under anhydrous conditions and at 0°C to a suspension of LAH (44 mg, 2 equiv.) in dry THF (5 mL). The reaction mixture was quenched with Glauber's salt ($Na_2SO_4 \cdot 10\ H_2O$, ca. 0.2 g) and the resulting slurry filtered through a pad of Celite®. The filtrate was evaporated on a rotary evaporator to give the desired amine as a colorless and odorless oil. It was, based on ^{1}H-NMR, 95% pure: R_f = 0.1 (silica-CH_2Cl_2/7% MeOH); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.65 (br s, 1H), 3.70 (s, 4H), 6.08 (s, 2H), 6.15 (s, 2H), 6.68 (s, 2H), 8.70 (br s, 2H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 45.6, 106.9, 108.2, 117.6, 129.9; LR-MS (EI, 180°C) *m/e* 175 (30.1, M^{+}), 158 (37.8), 108 (57.9, M^{+}-pyrrole), 95 (93.8, $C_5H_6N^{+}$), 80 (100, $C_5H_6N^{+}$), 68 (63.1, $C_4H_6N^{+}$); HR-MS (EI, 180°C) *m/e* calc'd for $C_{10}H_{13}N_3$: 175.11095, found 175.11107.

Procedures for the Preparation of Cyanopyrroles

The starting pyrrole (10 mmol) in a flask equipped with a septum, was dissolved under anhydrous conditions in a mixture of dry DMF (2 mL) and dry CH_3CN (10 mL), and the flask was cooled in an salt/ice bath to -5°C. Chlorosulfonylisocyanate (CSI) (1.1 equiv. for the preparation of mono-cyanopyrroles, 2.5 equiv. for the preparation of dicyanopyrroles) dissolved in dry CH_3CN (5 mL) was carefully syringed into the stirred solution. When no starting material was detectable by TLC (~15 min), the solution was quenched by pouring into aqueous Na_2CO_3 (100 mL, 5 % w/w). The resulting mixture was stirred for 1 h at room temperature and then extracted with $CHCl_3$ (3 x 50 mL). The organic extracts were combined and thoroughly washed with water, dried over Na_2CO_3 and evaporated to dryness. The residue was loaded onto a flash chromatography column (silica gel, 25 x 3 cm-$CHCl_3$) and the appropriate fractions were collected and evaporated to dryness to produce the purified cyanopyrroles

2-Cyano-3,4-diethylpyrrole (**12**). Prepared from 3,4-diethylpyrrole (**9**)[28] in 76 % yield (1.12 g) according to the general procedure as a slightly pink, coarse crystalline solid. An analytical sample was sublimed at 70°C/0.2 torr: mp = 133-134°C (sublimed); R_f = 0.39 (silica-CH_2Cl_2); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.98 (two overlapping signals separated by 1 Hz - tr, J = 7.5 Hz, 6H), 2.41 (d of q, J = 0.8, 7.5 Hz, 2H), 2.57 (q, 7.5 Hz, 2H), 6.65 (d, 2.5 Hz, 1H), 8.95 (br s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 14.6, 15.0, 18.0, 18.2, 98.6, 115.2, 120.8, 125.8, 136.5; LR-MS (EI, 150°C) 148 (29.8, M^+), 133 (100, M^+-CH_3), 118 (20.7, M^+-C_2H_6), 106 (10.4), 91 (9.9), 77 (16.5); HR-MS (EI, 150°C) *m/e* calc'd for $C_9H_{12}N_2$: 148.10005, found 148.10045; Anal. calcd for $C_9H_{12}N_2$: C, 72.94; H, 8.16; N, 18.90; found: C, 73.00; H, 8.27; N, 19.02.

2-Cyano-3,5-dimethyl-4-ethylpyrrole (**13**). Prepared in 69 % yield (1.02 g) from 3-ethyl-2,4-dimethylpyrrole (**10**) and 1.2 equiv. of CSI according to the general procedure. The crude product can be filtered after the hydrolysis step (48 h, 5°C). Either column chromatography (silica-CH_2Cl_2) or sublimation (110°C/760 torr) gives analytical pure material as a white solid or long, colorless needles, respectively. mp = 133-134° (sublimed material); R_f = 0.31 (silica-CH_2Cl_2/0.5% MeOH); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.04 (t, 3.6 Hz, 3H), 2.12 (s, 3H), 2.18 (s, 3H), 2.35 (q, 3.6 Hz, 2H), 8.40 (br s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 10.0, 11.4, 15.0, 17.3, 96.7, 115.5, 122.6, 130.4, 131.1; LR-MS (EI, 150°C) *m/e* c 148 (25.3, M^+), 133 (100, M^+-CH_3), 32 (63.8); HR-MS (EI, 150°C) *m/e* calc'd for $C_9H_{12}N_2$: 148.0005, found 148.0001; Anal. calcd for $C_9H_{12}N_2$: C, 72.94; H, 8.16; N, 18.90; found: C, 73.17; H, 8.23; N, 19.00.

3-Cyano-2,5-dimethylpyrrole (**14**). Prepared from 2,5-dimethylpyrrole (**11**) in 71 % yield (850 mg) as fine, colorless crystals. An analytical sample was sublimed at 70°C/0.2 torr: mp = 85.0°C; R_f = 0.63 (silica-CH_2Cl_2); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.18 (s, 3H), 2.35 (s, 3H), 5.95 (d, 1.5 Hz, 1H), 8.40 (br s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 12.0, 12.5, 90.0, 107.8, 118.0, 127.7, 136.7; LR-MS (EI, 150°C) 120 (52.5, M^+), 119 (100), 105 (13.9), 92 (12.4), 78 (9.3), 65 (8.9); HR-MS (EI, 150°C) *m/e* calc'd for $C_7H_8N_2$: 120.06875, found 120.06822; Anal. calcd for $C_7H_8N_2$: C, 69.97; H, 6.71; N, 23.31; found: C, 70.15; H, 6.44; N, 23.18.

2,5-Dicyano-3,4-diethylpyrrole (**15**). Prepared in 47 % yield (810 mg) from 3,4-diethylpyrrole (**9**) according to the general procedure, after the addition of the CSI, the mixture was refluxed for 1 h. Hydrolysis was accomplished over an extended period of time (12 h) on a steam bath: R_f = 0.4 (silica-CH_2Cl_2/2.5% MeOH); ^{1}H-NMR (200 MHz, acetone-d_6) δ 1.18 (t, 7.5 Hz, 6H), 2.56 (q, 7.5 Hz, 4H), 10.9

(br s, 1H); ^{13}C-NMR (50 MHz, acetone-d_6) δ 15.0, 18.2, 102.7, 104.6, 135.8; LR-MS (EI, 150°C) 173 (25.5, M^+), 158 (100, M^+-CH_3); HR-MS (EI, 150°C) *m/e* calc'd for $C_{10}H_{11}N_3$: 173.09529, found 173.09512; Anal. calcd for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N, 24.26; found: C, 69.62; H, 6.38; N, 24.00.

*3,4-Dicyano-2,5-dimethylpyrrole (**16**).* Isolated as off-white, fine plates and rods either as side product from the preparation of **14**, or in 62 % yield (900 mg), from 2,5-dimethylpyrrole (**11**) following the general procedure: mp = 242-244° (dried at 80°C/ 0.2 torr, 15 h); R_f = 0.27 (silica-CH_2Cl_2); ^{1}H-NMR (200 MHz, acetone-d_6) δ 2.35 (s, 6H), 11.2 (v br s, 1H); ^{13}C-NMR (50 MHz, acetone-d_6) δ 11.7, 93.00, 114.5, 138.9; LR-MS (EI, 150°C) 145 (46.8, M^+), 144 (100, M^+-H), 5.0 (11.7, $C_7H_7N_2^+$); HR-MS (EI, 150°C) *m/e* calc'd for $C_8H_7N_3$: 145.06400, found 145.06332; Anal. calcd for $C_8H_7N_3$: C, 66.19; H, 4.86; N, 28.95; found: C, 66.10; H, 4.76; N, 28.75.

Reductive coupling of 2-cyanopyrroles

(2-Pyrrolylmethene)-(2-pyrrolylmethyl)imine (4). 2-Cyanopyrrole (**5**) (20 mmol, 1.84 g) dissolved in dry THF (10 mL) was carefully added dropwise under anhydrous conditions into a cooled (0°C) and vigorously stirred suspension of LAH (25 mmol, 950 mg) in THF (30 mL) over 20 min. At the end of the addition, the reaction mixture was stirred for an additional hour at 0°C. Glauber's salt (Na_2SO_4·10 H_2O, ca. 2.0 g) was slowly added until gas evolution ceased. The resulting colorless thick slurry was filtered through a pad of Celite® and the filter cake thoroughly rinsed with $CHCl_3$ (ca. 50 mL). The combined filtrates were evaporated to dryness on a rotary evaporator to give an 85.5% yield of **4** as a tan solid. The analytical data given for this known compound supplement the data previously reported:[6] Shiny tan plates (EtOH/H_2O); mp = 157°C (155-157°C[10]); R_f = 0.16 (silica-CH_2Cl_2/5% MeOH); ^{1}H-NMR (200 MHz, acetone-d_6) δ 4.59 (s, 2H), 5.93 (s, 1H), 5.98 (t, *J* = 2.0 Hz, 1H), 6.14 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.42 (dd, *J* = 1.9, 2.0 Hz, 1H), 6.67 (narrow m, 1H), 6.91 (narrow m, 1H), 8.15 (s, 1H), 9.85 (br s, 1H), 10.65 (br s, 1H); the ^{1}H-NMR is strongly solvent dependent: ^{1}H-NMR (200 MHz, DMSO-d_6) δ 4.57 (s, 2H), 5.90 (m, 2H), 6.09 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.43 (dd, *J* = 1.9, 2.0 Hz, 1H), 6.62 (m, 1H), 6.81 (s, 1H), 8.10 (s, 1H), 10.67 (br s, 1H), 11.80 (br s, 1H);); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 4.75 (s, 2H), 6.03 (m, 1H), 6.12 (m, 1H), 6.21 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.44 (m, 1H), 6.62 (m, 1H), 6.71 (s, 1H), 8.20 (br s, 1H), 8.40 (br s, 1H), 2nd NH proton not observable < 15 ppm; ^{13}C-NMR (50 MHz, $CDCl_3$) δ = 56.7, 106.2, 108.5, 110.0, 115.3, 117.6, 122.5, 129.3, 129.8, 152.9; LR-MS (EI, 150°C) *m/e* 173 (63.6, M^+), 96 (86.1), 92 (89.2), 80 (100, $C_5H_6N^+$), 68 (50.5); HR-MS (EI, 150°C) *m/e* calc'd for $C_{10}H_{11}N_3$: 173.09529, found 173.09535; Anal. calcd for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N, 24.26; found: C, 69.40; H, 6.36; N, 24.11.

Reduction Experiments with Cyanopyrroles **7**, **12**, *and* **13**

Following a generalized procedure as outlined for the preparation of **4**, ca. 100 mg of the respective cyanopyrroles were reduced. The crude reaction mixtures were evaporated to dryness and dried under high vacuum at ambient temperature. The resulting oils or solids were taken up in $CDCl_3$ and the success of the experiments was judged, in addition to evaluation of the LR-MS of the crude mixtures, by the resulting ^{1}H- and ^{13}C-NMR spectra. The product ratios were determined from integration of the ^{1}H-NMR.

*Reduction of 2-cyano-1-methylpyrrole (**7**).* This reduction gave 2-(aminomethyl)-1-methylpyrrole (**8**) and a second product, in a ratio of 13:1, which is tentatively assigned structure **17**: ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.2, 3.8, 4.6, 6.5, 6.6, 8.2; *m/e* = 201. **8**: ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.82 (s, 2H), 5.95-6.1 (m, 2H), 6.58 (m, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 33.6, 38.1, 106.3, 106.6, 122.2, 134.2;

LR-MS (EI, 200°C) *m/e* 110 (53, M^+), 94 (100, M^+-NH_2).

Reduction of 2-cyano-3,4-diethylpyrrole (12). This reduction produced 2-(aminomethyl)-3,4-diethylpyrrole (**20**) and the imine linked dimer **18** in variable ratios between 3:2 and 2:1: ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.3-1.4 (m, -$CH_2\underline{CH_3}$ of **18** and **20**), 2.25-2.65 (m, -$\underline{CH_2}CH_3$ of **18** and **20**), 3.2 (br s, -NH_2 of **20**), 3.82 (s, -$\underline{CH_2}NH_2$ of **20**), 4.78 (s, =N-CH_2- of **18**), 6.5-6.6 (pyrrole-H of **18** and **20**), 8.30 (s, -$C\underline{H}$=N of **18**), 8.80 (br s, pyrrolylmethyl-NH_2 of **18**, the corresponding signal for the pyrrolylmethene-NH is observed at >12 ppm), 9.1 (br s, NH of **25**).

Reduction of 2-cyano-4-ethyl-3,5-dimethylpyrrole (13). This reduction led to the exclusive formation of the imine linked dimer **19**: ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.05-1.2 (m, 6H), 2.03 (s, 3H), 2.07 (s, 3H), 2.10 (s, 3H), 2.19 (s, 3H), 2.35-2.47 (m, 4H), 4.62 (s, 2H), 8.20 (s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 8.8, 9.1, 10.7, 11.1, 15.5, 15.8, 17.3, 17.7, 55.4, 113.2, 120.7, 121.8, 122.7, 123.0, 124.1, 126.7, 127.9, 150.6; LR-MS (EI, 200°C) *m/e* 283 (23, M^+-2H), 179 (20), 163 (82), 150 (40), 136 (100).

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